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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,137	MINKO ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-7 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 04/12/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a drug delivery composition comprising a genus of compounds characterized by suppressing antiapoptotic cellular defense, a genus of anticancer agents, a genus compounds which target the cell-surface, and a genus of compounds referred to as multifunctional carriers. Therefore, the claims encompass a genus of molecules defined solely by

their principal biological property, which is simply a wish to know the identity of any material with that biological property.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 8, lines 28-32) that composition of the invention include, but are not limited to, composition which contains at least two, three, or four of the following components, a multifunctional carrier, a cell-surface targeting moiety, an anticancer agent, or a suppressor of antiapoptotic cellular defense. With regards to a suppressor of antiapoptotic cellular defense, the specification teaches (page 9, lines 17-33) that a suppressor of antiapoptotic cellular defense specifically targets intracellular pathways responsible for resistance of cancer cells to chemotherapeutic agents thereby enhancing the activity of anticancer agents and includes, but is not limited to, BH3 peptides, BCL-2 antisense oligonucleotides, active portion of BCL-2 protein or an antibody which binds Serine-70. With regards to the cell-surface targeting moiety, the specification teaches (page 12, line 19 to page 13, line 27) that a cell surface targeting moiety is defined as an agent which specifically targets the complex drug delivery composition to a cancer cell and facilitates uptake into the cell, and includes, but is not limited to, moieties such as the following: peptide hormones such as bombesin, stomatostatin and luteinizing hormone-releasing hormone (LHRH); lectins and neoglycoconjugates; and antibodies/fragments thereof. With regards to multifunctional carrier components, the specification teaches (page 18, line 8 to page 19, line 6) that the multifunctional carrier components are typically a polymer having at least two of the following characteristics: providing multiple site for attachment of other components; functioning as a spacer; extending the half-life; and functioning to increase the molecular weight of the drug complex for enhanced targeting and include, but are not limited to, N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer, styrene-malienanhydride copolymer, polyethylene glycol (PEG) polypropylene

oxide, polyglutamic acid, dextran as well as liposomes or non-particles. With regards to the anticancer agent, the specification teaches (page 19, line 7 to page 21, line 2) that the anticancer agent includes, but is not limited to, a "laundry list" of possible anticancer agents ranging from cytotoxic agents to proteosome inhibitors. Thus, while the specification appears to contemplate that the drug delivery composition may comprise any one of the suppressors, anticancer agents, cell-surface targeting moieties or multifunctional carriers, the written description (specification, examples starting on page 33) only reasonably conveys a drug delivery composition comprising one species of compounds which suppress antiapoptotic cellular defense, i.e., BH3; one species of anticancer agent, i.e., CPT; one species of cell-surface targeting moiety; e.g., LHRH; and one species of multifunctional carriers, e.g., PEG. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the drug

delivery composition encompassed by the plethora of molecules described in the specification, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. A "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a drug delivery composition comprising one species of compounds which suppress antiapoptotic cellular defense, i.e., BH3; one species of anticancer agent, i.e., CPT; one species of cell-surface targeting moiety; e.g., LHRH; and one species of multifunctional carriers, e.g., PEG, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a complex drug delivery composition for treating cancer comprising at least the two of the following components: a) a suppressor of antiapoptotic cellular defense; b) an anticancer agent; c) a cell-surface targeting moiety; or d) a multifunctional carrier, wherein the at least two are a combination of either (a) and (b), (a) and (c), (a) and (d), (b) and (c), or (b) and (d), does not reasonably provide enablement for a complex drug delivery composition for treating cancer comprising at least (c) and (d) or a drug delivery composition for treating cancer comprising at least (c) and (d) which are the same, e.g., a cell-surface targeting moiety and a multifunctional carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims read on a complex drug delivery composition comprising at least two of the following components: a) a suppressor of antiapoptotic cellular defense; b) an anticancer agent; c) a cell-surface targeting moiety; or d) a multifunctional carrier, and a method of treating cancer using said complex drug delivery composition. The claims further include the limitation that the cell-surface targeting moiety and multifunctional carrier are the same. In the instant case, the terminology "at least two" implies that the composition must contain two of the components and may or may not contain any of the others. Thus, the claims may read on a drug delivery composition for treating cancer, wherein the composition comprises a cell-surface targeting moiety and a multifunctional carrier that may or may not be the same.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to a complex drug delivery composition for treating cancer comprising at least (c) and (d) or a drug delivery composition for treating cancer comprising at least (c) and (d) which are the same, e.g., a cell-surface targeting moiety and a multifunctional carrier. The specification teaches (page 8, lines 28-32 and page 9, lines 1-16) that compositions of the invention include, but are not limited to, compositions which contain at least two, three, or four of the following components, a

multifunctional carrier, a cell-surface targeting moiety, an anticancer agent, or a suppressor of antiapoptotic cellular defense which can be used for treating a variety of cancers. In addition, the speciation teaches (page 23, lines 28-32) that the multifunctional carrier and cell surface-targeting moiety may be the same molecule, e.g., a high molecular weight, water-soluble polymer. The specification further provides a variety of drug delivery compositions such as CPT-PEG (anticancer agent and multifunctional carrier/targeting moiety), CPT-PEG-BH3 (anticancer agent, multifunctional carrier/targeting moiety and antiapoptotic suppressor), CPT-PEG-LHRH (anticancer agent, multifunctional carrier and targeting moiety), and CPT-PEG-(BH3)(LHRH) (anticancer agent, multifunctional carrier, targeting moiety and antiapoptotic suppressor), as well as an examination of their anticancer effectiveness (beginning on page 33, Example 1 to page 45, Example 5, line 15 and page 47, Example 7). Thus, while the specification clearly teaches a drug delivery composition for treating cancer comprising at least either (a) and (b), (a) and (c), (a) and (d), (b) and (c), or (b) and (d) (as defined above), the specification appears to be silent on a drug delivery composition for treating cancer comprising (c) and (d) or a drug delivery composition for treating cancer comprising (c) and (d) which are the same, e.g., a cell-surface targeting moiety and a multifunctional carrier.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to treating cancer with a drug delivery composition comprising at least a cell-surface targeting moiety and a multifunctional carrier or a cell-surface targeting moiety and multifunctional carrier which are the same, and applicant has not enabled all of these types of drug delivery compositions because it has not been shown that a drug delivery composition comprising either a cell-surface targeting moiety, i.e., an antibody or lectin, and a multifunctional carrier, i.e. PEG or a multifunctional carrier/targeting moiety, i.e., a high molecular weight water soluble polymer, are capable of functioning as to that which is being disclosed. For example, Jain (Scientific American July 1994) discloses barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1

paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutics molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Further, in the late 80's, Dillman (Annals of Internal Medicine, Volume 111, pages 592-603, 1989) summarized (see abstract) the status of in-vivo use of monoclonal antibodies for treating cancer wherein despite advances in biotechnology, many major hurdles persist including tumor cell heterogeneity, lack of cytotoxicity, and the development of human anti-mouse antibodies (HAMA). More recently, Weiner (Seminars Oncology, Vol. 26, No.4, 1999, pages 41-50) provided an overview of monoclonal antibody of therapy including some promising activity, however major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. This includes impaired distribution and delivery of antibody to the tumor site, inadequate trafficking of potential cellular effectors to tumor, antigenic heterogeneity, shed or internalized targets, insufficient target specificity, and induction of HAMA (page 43). While it is well known in the art, as exemplified in the specification (page 18, lines 27-30 and 23, lines 8-14), that high molecular weight polymers such as PEG can be used as both tumor targeting agents and as multifunctional carriers conjugated to drugs which increase the drugs half-life from minutes to hours, the prior art appears to be silent on the effectiveness of high molecular weight polymers alone for the treatment of cancer. Further, treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art such as cancer therapy.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Minko et al. (int. J. Cancer 2000; 86: 108-117, IDS).

Minko et al. teach a drug delivery composition for treating cancer comprising the anticancer agent doxorubicin linked through an oligopeptide spacer, e.g., GFLG, to a HPMA copolymer carrier and a two-step method of producing the composition (page 108, 2nd column, *Drugs*). With regards to the compositions preparation, the reference teaches (page 108, 2nd column, Drugs) that the first step involves radical precipitation copolymerization of HPMA and N-methacryloylglycylphenyl-analylleucylglycine p-nitro ester which generates the HPMA-GFLG precursor, and the second step involves binding DOX via aminolysis to the polymer precursor. Minko et al. further teach (page 110, 1st column, *Antitumor activity*) that the administration of P(GFLG)-Dox to tumor bearing mice dramatically decreased tumor size 28 times in sensitive A2780 tumor and 18 times in resistant A2770/Ad tumor when compared to controls. Moreover, the reference teaches (page 110, 2nd column, *Doxorubicin accumulation*) that the DOX concentration in tumors was 45-250 times higher than in other organs following the administration of P(GFLG)-DOX. Although Minko et al. does not specifically teach that the oligopeptide spacer is a scaffold, the claimed limitation is an inherent property of an oligopeptide because the specification discusses (page 29, line 33 to page 30, line 1) that a scaffold is a peptide of 1 to 10 amino acid residues. Thus, the claimed drug delivery composition appears to be the same as the prior art. Furthermore, while Minko et al. does not specifically teach that the multifunctional carrier and cell-surface targeting moieties are the same, the

claimed functional limitation would be an inherent property because as the specification teaches (page 23, lines 26-32) that a multifunctional carrier and cell surface targeting moiety are the same when they are a high molecular weight, water soluble polymer, for example, HPMA copolymer-bound DOX (P-DOX). In the instant case, the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Lu et al. (J. Controlled Rel. 1/17/2002; 78: 165-173).

Lu et al. teach (abstract) a drug delivery composition for treating cancer comprising polymerizable carrier antibody Fab' fragment as the targeting agent linked to an anticancer agent such as mesochlorin e_6. With regards to the polymerizable antibody Fab' fragment, the reference teaches (beginning on page 167, 1st column, 1st full paragraph) that the polymerizable antibody fragments were prepared by polymerizing an antibody fragment comprising a spacer, such as PEG, with HPMA. Lu et al. further provide (page 167, 2nd column, 2nd paragraph and page 168, Scheme 2) a method of producing the drug delivery composition comprising combining an anticancer agent comprising a tetrapeptide spacer with the HPMA and the polymerizable antibody. Moreover, the reference teaches (page 168, 2nd column, 2nd paragraph and page 169, Figure 3) a method of treating cancer comprising administering an effective amount of the drug delivery composition so that the tumor showed signs of regression. Although Lu et al. does not specifically teach that the oligopeptide spacer is a scaffold, the claimed limitation is an inherent property of an oligopeptide because the specification discusses (page 29, line 33 to page 30, line 1) that a scaffold is a peptide of 1 to 10 amino acid residues. Thus, the claimed drug delivery composition appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the

contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Trouet et al. (WO 01/91798, 2001).

Trouet et al. teach a prodrug for treating cancer comprising a biologically active entity linked to a masking moiety via a linking moiety (abstract). With regards to the biologically active entity, the WO document teaches (page 60, claim 51 of the WO document) that the biologically active entity includes, but is not limited to, BH3 peptides and anticancer agents such as anthracyclines, doxorubicin and camptothecins. With regards to the linking group, Trouet et al. teach (page 2, lines 17-23) that the linking moieties are preferably peptides having the amino acid sequence of $(Leu)_y(Ala\text{-}Leu)_xAla\text{-}Leu$ and $(Leu)_y(Ala\text{-}Leu)_xAla\text{-}Phe$, where y is 0 or 1 and x is 1, 2, or 3. With regards to the masking moiety, the WO document teaches (page 5, lines 21-33, page 15, lines 16-35 and page 32, lines 14 +) that the masking moiety may have biological activity such that prodrug is a dual prodrug and further, comprise large molecular weight biologically inert molecules such as PEG or HPMA. Trout et al. further teach (page 6, lines 18-24) a method of treating cancer comprising administering the prodrug to an animal in an effective amount to shrink or eradicate the tumor. Furthermore, the WO document teaches (page 35, lines 24+) a method of making the prodrug comprising condensing the masking moiety and biological entity with the linking moiety. Although Trouet et al. does not specifically teach that the linking moiety is a scaffold, the claimed limitation is an inherent property of a linking moiety because the specification discusses (page 29, line 33 to page 30, line 1) that a scaffold is a peptide of 1 to 10 amino acid residues. Thus, the claimed drug delivery composition appears to be the same as the prior art. Furthermore, while Trouet et al. does not specifically characterize the high molecular weight biologically inert polymer such as PEG or HPMA as a multifunctional carrier or a cell-surface targeting moieties or as being the same, the claimed functional limitation would be an inherent property because as the specification teaches (page 23, lines 8-32) high molecular weight water-soluble polymers have been shown to preferentially accumulate in solid tumors such that they may act as both the multifunctional carrier and cell surface targeting moiety. Lastly, even though Trouet et al. does not explicitly teach that BH3 peptide is a

suppressor of antiapoptotic cellular defense, the claimed limitation would be an inherent characteristic of a BH3 peptide because the specification discusses (page 9, lines 17-25) that exemplary antiapoptotic cellular defense components include BH3 peptides. In this case, the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
4/3/06